Amendments to the Claims:

This listing of claims will replace all prior listings, and versions, of claims in the application.

Listing of Claims

1. (currently amended) A method comprising:

1) screening a plurality of compounds for potential development as a candidate cognitive enhancer compounds by

2) determining the ability of said compounds to enhance cyclic adenosine monophosphate (cAMP) response element binding protein (CREB) pathway function wherein said screening and determining comprises the steps of:

a) contacting host cells comprising an indicator gene operably linked to a cAMP response element (CRE) promoter with a test compound and with a suboptimal dose of a CREB function stimulating agent simultaneously or sequentially wherein said CREB function stimulating agent is forskolin;

b) determining indicator activity in said host cells which have been contacted with said test compound and with said CREB function stimulating agent;

c) determining indicator activity in said host cells which have been contacted with said CREB function stimulating agent alone;

d) determining indicator activity in said host cells which have been contacted with said test compound alone; and

e) determining indicator activity in said host cells which have not been contacted with said test compound or said CREB function stimulating agent;

f) [[c)]] comparing the indicator activity determined in ~~step b)~~ each of steps b) through e) ~~with the indicator activity in control cells which have been contacted with said CREB function stimulating agent and which have not been contacted with said test compound~~;

g) [[d)]] selecting said test compound if:

i) the indicator activity determined in step b) is increased relative to the indicator activity determined in step c); ~~said control cells which have been contacted with said CREB function stimulating agent and which have not been contacted with said test compound;~~ and

ii) the indicator activity determined in step d) is not significantly different relative to the indicator activity determined in step e); ~~in control cells which have not been contacted with said CREB function stimulating agent and which have not been contacted with said test compound is not significantly different relative to the indicator activity in control cells which have not been contacted with said CREB function stimulating agent and which have not been contacted with said test compound;~~

h) [[e)]] repeating steps a) to g) ~~to d)~~ with a range of different concentrations of said test compound selected in step g) [[d)]]; and

i) [[f)]] selecting said test compound if:

i) the indicator activity determined in step b) is increased relative to the indicator activity determined in step c) ~~is increased~~ in the range of different concentrations of ~~for~~ said test compound ~~relative to the indicator activity in said control cells which have been contacted with said CREB function stimulating agent and which have not been contacted with said test compound~~; and

ii) the indicator activity determined in step d) is not significantly different relative to the indicator activity determined in step e) in the range of different concentrations of said test compound, ~~in control cells which have not been contacted with said CREB function stimulating agent and which have been introduced said range of different concentrations of said test compound is not significantly different relative to the indicator activity in control cells which have not been~~

~~contacted with said CREB function stimulating agent and which have not been contacted with said test compound,~~ and

3) identifying said test compound as a candidate cognitive enhancer compound if said test compound is selected in steps g) and i) ~~d) and f)~~.

2. (original) The method of claim 1 wherein said host cells are contacted with said test compound prior to contact with said CREB function stimulating agent.

3. (original) The method of claim 1 wherein said host cells are human neuroblastoma cells.

4. (original) The method of claim 1 wherein said indicator gene encodes luciferase.

5. (cancelled)

6. (currently amended) The method of claim 4 wherein steps a) to g) ~~to d)~~ are repeated with a range of four different concentrations of the said test compound selected in step g). [[d).]]

7. (currently amended) The method of claim 1further comprising the steps of:

j) [[g)]] contacting cells of neural origin with said identified candidate cognitive enhancer compound and with a suboptimal dose of a CREB function stimulating agent simultaneously or sequentially, wherein said cells of neural origin are different from the host cells of step a);

k) [[h)]] assessing endogenous CREB-dependent gene expression in said cells of neural origin which have been contacted with said candidate cognitive enhancer compound and with said CREB function stimulating agent; ~~and~~

l) assessing endogenous CREB-dependent gene expression in said cells of neural origin which have been contacted with said CREB function stimulating agent alone; and

m) [[i)]] comparing endogenous CREB-dependent gene expression assessed in steps k) and l), ~~step h) with endogenous CREB-dependent gene expression in control cells which have been contacted with said CREB function stimulating agent and which have not been contacted with said candidate cognitive enhancer compound,~~ wherein a difference in the endogenous CREB-dependent gene

expression in step k) [[h)]] compared to the endogenous CREB-dependent gene expression in step l) ~~control cells~~ confirms that said compound is a candidate cognitive enhancer compound, thereby identifying said cognitive enhancer compound as a confirmed candidate cognitive enhancer compound.

8. (previously presented) The method of claim 7 wherein said cells of neural original are contacted with said candidate cognitive enhancer compound prior to contact with said CREB function stimulating agent.

9. (original) The method of claim 7 wherein said cells of neural origin are neurons.

10. (original) The method of claim 9 wherein said neurons are primary hippocampal cells.

11. (cancelled)

12. (currently amended) A method comprising

1) screening a plurality of candidate cognitive enhancer compounds by

a) contacting cells of neural origin with a candidate cognitive enhancer compound and with a suboptimal dose of a cyclic adenosine monophosphate (cAMP) response element binding protein (CREB) function stimulating agent simultaneously or sequentially;

b) assessing endogenous CREB-dependent gene expression in said cells of neural origin which have been contacted with said cognitive enhancer compound and with said CREB function stimulating agent;

c) assessing endogenous CREB-dependent gene expression in said cells of neural origin which have been contacted with said CREB function stimulating agent alone;

d) [[c)]] comparing endogenous CREB-dependent gene expression assessed in step b) with endogenous CREB-dependent gene expression assessed in step c); ~~control cells which have been contacted with said CREB function stimulating agent and which have not been contacted with said candidate cognitive enhancer compound and~~

2) identifying candidate cognitive enhancer compounds for further study as a cognitive enhancer if said endogenous CREB-dependent gene expression in step b) is significantly increased relative to said endogenous CREB-dependent gene expression in step c). ~~cells contacted in step b) show significantly more CREB-dependent gene expression than said endogenous CREB-dependent gene expression in control cells which have not been contacted with said CREB function stimulating agents and which have not been contacted with said candidate cognitive enhancer compound.~~

13. (previously presented) The method of claim 12 wherein said cells of neural origin are contacted with said candidate cognitive enhancer compound prior to contact with said CREB function stimulating agent.

14. (original) The method of claim 12 wherein said cells of neural origin are neurons.

15. (original) The method of claim 14 wherein said neurons are primary hippocampal cells.

16. (cancelled)

17. (withdrawn) A method for assessing the effect on long term memory formation in an animal of a candidate compound for enhancing CREB pathway function comprising the steps of:

a) administering said candidate compound to be assessed to said animal;

b) training said animal administered said compound under conditions appropriate to produce long term memory formation in said animal;

c) assessing long term memory formation in said animal trained in step b); and

d) comparing long term memory formation assessed in step c) with long term memory formation produced in the control animal to which said candidate compound has not been administered.

18. (withdrawn) The method of claim 17 wherein said mammal is a mammal

19. (currently amended) A method comprising

1) screening a plurality of compounds for potential use as a cognitive enhancer by assessing said compounds' ability to enhance cyclic adenonsine

monophosphate (cAMP) response element binding protein (CREB) pathway function comprising the steps of:

a) contacting host cells comprising an indicator gene operably linked to a cAMP response element (CRE) promoter with a test compound, thereby producing a test sample;

b) contacting the test sample produced in step a) with a suboptimal dose of a CREB function stimulating agent wherein said CREB function stimulating agent is forskolin;

c) determining indicator activity in said host cells which have been contacted with said test compound and with said CREB function stimulating agent;

d) determining indicator activity in said host cells which have been contacted with said CREB function stimulating agent alone;

e) determining indicator activity in said host cells which have been contacted with said test compound alone; and

f) determining indicator activity in said host cells which have not been contacted with said test compound or with said CREB function stimulating agent;

g) ~~(d)~~ comparing the indicator activity determined in ~~step c)~~ each of steps c) through f) ~~with the indicator activity in control cells which have been contacted with said CREB function stimulating agent and which have not been contacted with said test compound~~;

h) [[e)]] selecting said test compound if:

i) the indicator activity determined in step c) [[b)]] is increased relative to the indicator activity determined in step d); ~~increased relative to the indicator activity in said control cells which have been contacted with said CREB function stimulating agent and which have not been contacted with said test compound;~~ and

ii) the indicator activity determined in step e) is not significantly different than the indicator activity determined in step f); ~~in~~

~~in control cells which have not been contacted with said CREB function stimulating agent and which have been contacted with said test compound is not significantly different relative to the indicator activity in control cells which have not been contacted with said CREB function stimulating agent and which have not been contacted with said test compound~~;

i) [[f)]] repeating steps a) to g) [[e)]] with a range of different concentrations of said test compound selected in step h) [[e)]];

j) [[g)]] selecting said test compound as a candidate if:

i) the indicator activity determined in step c) is increased relative to the indicator activity determined in step d) in the range of different concentrations of ~~for~~ said test compound ~~relative to the indicator activity in said control cells which have been contacted with said CREB function stimulating agent and which have not been contacted with said test compound~~; and

ii) the indicator activity determined in step e) is not significantly different than the indicator activity determined in step f) in the ~~in control cells to which have not been contacted with said CREB function stimulating agent and which have been introduced said~~ range of different concentrations of said test compound ~~is not significantly different relative to the indicator activity in control cells which have not been contacted with said CREB pathway function stimulating agent and which have not been contacted with said test compound, thereby selecting a candidate compound~~;

k) [[h)]] contacting cells of neural origin with said candidate compound selected in step j) [[g)]] and with a suboptimal dose of a CREB function stimulating agent;

l) [[i)]] assessing endogenous CREB-dependent gene expression in the cells of neural origin which have been contacted with said candidate compound and with said CREB function stimulating agent;

m) assessing endogenous CREB-dependent gene expression in the cells of neural origin which have been contacted with said CREB function stimulating agent alone;

n) assessing endogenous CREB-dependent gene expression in the cells of neural origin which have been contacted with said cognitive enhancer compound alone;

o) assessing endogenous CREB-dependent gene expression in the cells of neural origin which have not been contacted with said CREB function stimulating agent or with said cognitive enhancer compound

p) [[j)]] comparing endogenous CREB-dependent gene expression assessed in each of steps l)-o) ~~with endogenous CREB-dependent gene expression in control cells which have been contacted with said CREB function stimulating agent and which have not been contacted with said candidate compound~~;

q) [[k)]] selecting said candidate compound if:

i) endogenous CREB-dependent gene expression assessed in step l) [[i)]] is increased relative to endogenous CREB-dependent gene expression assessed in step m); and

ii) endogenous CREB-dependent gene expression assessed in step n) ~~in control cells which have not been contacted with said CREB function stimulating agent and which have been contacted with said candidate compound~~ is not significantly different relative to the endogenous CREB-dependent gene expression assessed in step o) ~~in control cells which have not been contacted with said CREB function stimulating agent and which have not been contacted with said candidate compound, thereby selecting a confirmed candidate compound~~;

2) identifying said candidate cognitive enhancer compound as a confirmed candidate cognitive enhancer compound if said compound is selected in steps h), j), and q). ~~e), g), and k).~~

20. (original) The method of claim 19 wherein said host cells are human neuroblastoma cells and said cells of neural origin are neurons.

21. (original) The method of claim 20 wherein said neurons are primary hippocampal cells.

22. (original) The method of claim 19 wherein said indicator gene encodes luciferase.

23. (cancelled)

24. (previously presented) The method of claim 19 wherein steps a) to e) are repeated with a range of four different concentrations of said test compound selected in step e).

25. (withdrawn) The method of claim 19 wherein said animal is a mammal.